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Reducing parental trauma and stress in neonatal intensive care: systematic review and meta-analysis of hospital interventions

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Abstract

Objective To classify NICU interventions for parental distress and quantify their effectiveness.

Study design We systematically reviewed controlled studies published before 2017 measuring NICU parental distress, defined broad intervention categories, and used random-effects meta-analysis to quantify treatment effectiveness.

Results Among 1643 unique records, 58 eligible trials predominantly studied mothers of preterm infants. Interventions tested in 22 randomized trials decreased parental distress ($p < 0.001$) and demonstrated improvement beyond 6 months ($p < 0.005$). In subgroup analyses, complementary/alternative medicine and family-centered instruction interventions each decreased distress symptoms ($p < 0.01$), with fathers and mothers improving to similar extents. Most psychotherapy studies decreased distress individually but did not qualify for meta-analysis as a group.

Conclusion NICU interventions modestly reduced parental distress. We identified family-centered instruction as a target for implementation and complementary/alternative medicine as a target for further study. Investigators must develop psychosocial interventions that serve NICU parents at large, including fathers and parents of full-term infants.

Introduction

The hospitalization of one's newborn in a neonatal intensive care unit (NICU) represents a potentially traumatic event for parents [1, 2]. Individual parents exhibit profoundly heterogeneous psychological responses to the NICU

hospitalization of their newborn infant as determined by multiple known and unknown infant, parent, and social factors [3].

In the NICU environment, parents may feel their parenting role diminished as a result of professionals and policies governing interactions between parents and their infants [4]. Parents may perceive the threat of their child's disability or death when they see their newborn attached to medical devices and experiencing suffering or physiologic instability [5]. As a consequence of these experiences, NICU parents can suffer from aspects of stress- and trauma-related distress such as anxiety, stress, or post-traumatic stress [6, 7]. Prolonged postnatal distress harms parents' mental health, disrupts the parent–infant relationship, and impairs children's functioning and social-emotional development in the future [8–10].

The general population faces a tangible risk of NICU-related parental distress. In the United States, about one in ten newborns receives care in an NICU [11]. Many NICU parents experience some postnatal symptoms of post-traumatic stress [12]. A meta-analysis of mothers of high-risk newborns reports that 18.5% meet diagnostic criteria for post-traumatic stress disorder (PTSD) after birth, compared with 4% of post-partum mothers in the community [13]. The prevalence of postnatal distress among NICU

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fathers, as reported in single-site studies, ranges from 8 to 47%, compared to a baseline postnatal paternal rate of 6–8.7% [14–18].

Even though experts and families recognize the burden of NICU-related distress and agree on the need for psychosocial support, standard practices for screening or supporting NICU parents are not in place universally [12, 19]. Furthermore, it remains challenging for clinicians and investigators to choose the most promising approaches from among the eclectic collection of treatments that have been studied.

No prior review has comprehensively synthesized studies of interventions to reduce distress in NICU parents at large. Previous systematic reviews selected narrow scopes that limited their applicability across varied patient populations, treatment modalities, and psychological outcomes [20–24]. First, few reviews examined the effect of interventions on fathers' distress symptoms, even though NICU fathers experience birth-related psychological distress [25]. Second, prior reviews predominantly assessed distress in parents of premature or very low birth weight infants, even though parents of critically ill full-term newborns are similarly susceptible to psychological distress [26]. Third, no review has quantitatively synthesized the effect of diverse NICU interventions on parental PTSD using meta-analysis.

We undertook this systematic review and meta-analysis of NICU interventions for stress- and trauma-related parental distress to achieve the following aims: (1) to characterize the populations, interventions and outcomes reported in controlled studies; (2) to classify interventions targeting NICU-parental distress; (3) to estimate the overall effectiveness of interventions during NICU hospitalization and long-term; and (4) to compare treatment effectiveness among intervention classes, between mothers and fathers, and between short- and long-term outcomes. Through this analysis, we sought to identify the most promising treatment approaches for implementation by health systems and further study by investigators.

Methods

We adhered to a predetermined protocol that specified study search strategy, eligibility criteria, methods of analysis, outcome variables, and effect direction [27]. We describe the full methods in the supplemental materials.

Study search and selection

We searched PubMed, PsycINFO, CINAHL, and SCOPUS for studies published before 2017 using terms for the following concepts: hospitalized infants, parents, stress,

anxiety, PTSD, and intervention. (Complete search terms are listed in supplemental materials.)

Three reviewers eliminated duplicate records and reviewed full-text reports to identify studies eligible for inclusion.

Study eligibility criteria

In the systematic review, we included English-language experimental studies (1) enrolling parents of infants admitted to an NICU, (2) testing interventions during or pertaining to the hospitalization, (3) reporting post-intervention parental anxiety, stress, or post-traumatic stress, and (4) comparing outcomes between NICU parents exposed to an intervention vs. NICU parents exposed to a placebo treatment or usual care.

In order to synthesize study effects homogeneously, we excluded from review observational studies and studies with an exclusively pre-post design lacking a distinct control group. To decrease heterogeneity, we excluded from the meta-analysis studies that failed to report outcomes as unadjusted scores.

Data collection

From each report included in the systematic review, we extracted information pertaining to the study, subjects, intervention, and outcomes. We separately collected and analyzed data for mothers and fathers when they were reported distinctly within a single study. We classified interventions into broad categories. Local experts in serious pediatric illness and parental adjustment corroborated the face validity of our intervention typology.

To account for the highly variable trajectories of distress symptoms individuals experience when faced with potentially traumatic events, we chose two time points for quantitative synthesis: (1) the latest in-hospital measurement, and (2) the most distal measurement reported [2]. Despite wide variability in individual distress patterns, on average, parental distress symptoms are highest during the hospitalization and decline over time [28]. To assess long-term treatment effects, we collected distress measurements most distal in time to interventions as our primary outcome. Therefore, when analyzing the primary outcome, for trials publishing serial reports from a single sample, we only included the report presenting the furthest time point; and for studies reporting outcomes at multiple time points, we only synthesized data from the furthest time point. To assess treatment effects during NICU hospitalization, a secondary outcome was the latest in-hospital distress measurement prior to NICU discharge, which we collected separately for studies reporting results at multiple time points.

Summary measures

From studies eligible for meta-analysis, we collected anxiety and stress- or trauma-related distress scores. We included anxiety symptoms because, prior to the fifth and current edition of the Diagnostic and Statistical Manual of Mental Disorders, stress- and trauma-related disorders were sub-classified as anxiety disorders [29].

The primary measure of treatment effect for meta-analysis was the standardized mean difference (SMD) in distress symptoms between the intervention and control groups (i.e., control subtracted from intervention). We classified negative SMD values as favoring intervention. We reversed signs when necessary to yield consistent inter-group SMDs.

We aggregated measures of stress, trauma, and anxiety for meta-analysis. To harmonize numerous psychometric instruments for distress symptoms, we calculated the Z-score ($[\text{study mean} - \text{group mean}] \div \text{group standard deviation}$) and the standardized standard deviation ($\text{study standard deviation} \div \text{group standard deviation}$) for each reported instrument. For studies reporting the results of multiple instruments from the same subjects, we calculated weighted averages of Z-scores to provide composite measurements of distress for each study group.

Meta-analysis

We predicted a lack of common treatment effect among studies testing heterogeneous interventions. Therefore, to quantify the overall effectiveness of interventions, we employed the random effects meta-analysis method of DerSimonian and Laird [30]. We assessed heterogeneity among study effect estimates using both Higgins' I^2 and Cochran's Q statistics. We used funnel plots and Egger's test to detect reporting bias pertaining to the relationship between sample size and effect size. We expected randomized studies to have lower risk of bias than non-randomized experimental studies; therefore, they were analyzed separately.

We carried out meta-analysis procedures in Stata/SE version 14 (Stata Corp., College Station, TX) using the following programs: *metan* to conduct random-effects meta-analysis, *metafunnel* to generate funnel plots, and *metabias* to carry out Egger's test [31].

Additional analyses

We conducted predetermined subgroup analyses of randomized studies eligible for meta-analysis to assess the comparative effectiveness of interventions (1) among intervention classes, (2) between mothers and fathers, and (3) on short-term and long-term outcomes. We conducted

Fig. 1 Study selection flow diagram

one post-hoc sensitivity analysis to determine the overall and subgroup effect sizes after excluding studies conducted in Iran that, as a group, were outliers favoring intervention compared to studies conducted elsewhere.

Results

Study selection

A study selection flow diagram (Fig. 1) illustrates the process we undertook to select 58 controlled studies of interventions for NICU parental distress for systematic review (references listed in supplemental materials). Among those, we quantitatively synthesized 23 randomized, and 10 non-randomized, controlled studies.

Table 1 Controlled studies of interventions to reduce NICU parental distress

First author	Year	Country	Subjects enrolled	Parents ^a	Randomized	Intervention	Distress measures	Instruments	Significant difference ^b
Changing NICU medical care									
Meyer ^c	1994	USA	34	m	Yes	Individualized interventions like observing newborn behavior assessment or participating in caregiving or discharge preparation for mothers of preterm infants.	Stress	PSS-NICU	+
Rieger	1995	Australia	118	m	No	NEDP focused on discharge and transition for mothers of preterm infants.	Anxiety	STAI	0
Preyde ^c	2003	Canada	59	m	No	Parent-to-parent support groups for mothers of preterm infants	Anxiety	STAI, PSS-NICU	+
Singh	2003	India	200	f	No	Fathers were permitted to visit the bedside and offered clinical updates in a NICU where the standard policies prohibited fathers.	Anxiety	Original survey	+
Koh ^{c,d}	2007	Australia	32	m	Yes	Parents were given an audiotape of their initial conversations with their infants' neonatologist.	Anxiety	STAI	0
Erdevic ^c	2009	Turkey	49	m	No	Mothers and preterm infants were hospitalized together.	Stress	PSI	0
Liu	2010	Taiwan	70	m + f	No	Support groups provided parents of preterm infants with empowerment strategies.	Stress	Perceived Stress Scale	0
Pineda ^c	2012	USA	81	m	No	Preterm newborns were assigned single-patient NICU rooms vs. open-bay beds.	Anxiety, Stress	STAI, PSS-NICU, PSI	0
O'Brien ^c	2013	Canada	56	m	No	FIC tightly incorporated mothers in their preterm infants' care.	Stress	PSS-NICU	+
Weiss ^c	2013	Denmark	134	m + f	Yes	GFCC helped parents of preterm infants manage distress and care decisions.	Stress	PSS-NICU	0
Clarke-Pounder ^{c,d}	2015	USA	19	m	Yes	NICU DMT elicited parental values and preferences about medical decisions.	Anxiety	STAI	–
Complementary/alternative medicine									
Barry ^c	2001	USA	38	m	Yes	Mothers wrote daily about their most emotional NICU experiences.	PTSD	IES, SCL-90-R	+
Feijo ^{c,d}	2006	USA	40	m	Yes	Infant massage by mothers.	Anxiety	STAI	+
Lai	2006	Taiwan	30	m	Yes	Mother–preterm-infant dyads were exposed to music during kangaroo care.	Anxiety	STAI	+
Flacking	2013	Sweden	300	m	No	Skin-to-skin contact with mothers of preterm infants in co-care facilities.	Stress	PSI	0
Haddad-Rodrigues ^{c,d}	2013	Brazil	29	m	Yes	Weekly acupuncture on ears of mothers of preterm infants.	Anxiety	STAI	0
Holditch-Davis	2014	USA	240	m	Yes	Mothers provided kangaroo care or auditory, tactile, visual, vestibular stimulation to their preterm infants.	Anxiety, PTSD	STAI, PPQ	+
Kadivar ^c	2015	Iran	70	m	No	Mothers performed narrative writing at least three times within 10 days of their preterm infant's hospitalization.	Stress	PSS-NICU	+

Table 1 (continued)

First author	Year	Country	Subjects enrolled	Parents ^a	Randomized	Intervention	Distress measures	Instruments	Significant difference ^b
Möreluis	2015	Sweden	37	m + f	Yes	Mother-preterm-infant skin-to-skin contact.	Stress	SPSQ	0
Afand ^c	2016	Iran	70	m	No	Preterm infants massage by mothers.	Anxiety	STAI	+
Fotiou ^c	2016	Greece	59	m + f	Yes	Parents of preterm infants practiced deep breathing, progressive muscle relaxation, and guided imagery.	Anxiety, Stress	STAI, Perceived Stress Scale	+
Sharifnia	2016	Iran	60	m	Yes	Mothers of premature infants listened to Tavassol prayer daily.	Anxiety, Stress	DASS	0
Cho	2016	South Korea	40	m	No	Kangaroo care with preterm infants.	Stress	PSS-NICU	+
Family-centered instruction									
Culp	1989	USA	14	m + f	No	Parents learned assessment of premature infant behavior.	Anxiety	STAI	+
Cobiella	1990	USA	30	m	Yes	Educational videotapes taught mothers to address anxiety and confidently care for their preterm infants.	Anxiety, Stress	STAI, PSS-NICU	+
Melnik ^{c,d}	2001	USA	42	m	Yes	COPE taught parents how to integrate into their preterm, low-birth weight infants' care.	Stress	PSS-NICU	0
Browne	2005	USA	84	m	Yes	Mothers were taught to elicit their preterm infants' normal reflexes.	Stress	PSI	+
Kaarsen ^c	2006	Norway	235	m + f	Yes	MITP taught parents to observe preterm infant's state and to use positive stimulation.	Stress	PSI	+
Melnik ^{c,d}	2006	USA	386	m + f	Yes	COPE taught parents how to integrate into their preterm infants' care.	Anxiety, Stress	STAI, PSS-NICU	+
Glazebrook	2007	UK	199	m	Yes	PBIP taught parents to identify preterm infant cues.	Stress	PSI	0
Van de Pal	2007	Netherlands	283	m + f	Yes	NIDCAP modified preterm infants' environment and caregiving.	Stress	PSS-NICU	0
Turan ^{c,d}	2008	Turkey	76	m + f	Yes	30-min parent education program about their preterm infant and the NICU.	Stress	PSS-NICU	+
Van de Pal ^c	2008	Netherlands	128	m + f	Yes	NIDCAP modified preterm infants' environment and caregiving.	Stress	PSI	0
Carvalho	2009	Brazil	59	m	Yes	Mothers of preterm infants received psychological support through audiovisual and print materials.	Anxiety	STAI	0
Newnham ^c	2009	Australia	63	m	Yes	MITP taught parents to observe preterm infant's state and to use positive stimulation.	Stress	PSI	+
Zelkowitz ^d	2011	Canada	98	m	Yes	Cues & Care taught mothers to address distress in their VLBW infants and themselves.	Anxiety, PTSD	STAI, PPQ	0
Franck ^{c,c,d}	2011	USA	169	m + f	Yes	Parents received a pain information booklet and instructions on preterm infant comforting techniques.	Stress	PSS-NICU	0
Feeley ^c	2012	Canada	96	m	Yes	Cues & Care taught mothers to address distress in their VLBW infants and themselves.	Anxiety, PTSD	STAI, PPQ	0

Table 1 (continued)

First author	Year	Country	Subjects enrolled	Parents ^a	Randomized	Intervention	Distress measures	Instruments	Significant difference ^b
Ravn ^c	2012	Norway	100	f	Yes	MITP taught parents to observe preterm infant's state and to use positive stimulation.	Stress	PSI	0
Borimnejad ^c	2013	Iran	140	m	No	COPE taught parents how to integrate into their preterm infants' care.	Stress	PSS-NICU	+
Lee ^c	2013	Taiwan	69	f	No	Fathers received a booklet about their premature infant's care and individualized guidance from a nurse.	Stress	PSS-NICU	+
Matricardi	2013	Italy	42	m+f	Yes	A physical therapist taught parents to observe their preterm infant's behavior and provide positive stimulation during therapy sessions.	Stress	PSS-NICU	+
Borghini ^c	2014	Switzerland	78	m	Yes	Parents learned about their preterm infant's behaviors and their own reactions to them with the help of a therapist.	PTSD	PPQ	0
Landsem ^c	2014	Norway	234	m+f	Yes	MITP taught parents to observe preterm infant's state and to use positive stimulation.	Stress	PSI	+
Mianaei ^c	2014	Iran	90	m	Yes	COPE taught parents how to integrate into their preterm infants' care.	Anxiety, Stress	STAI, PSS-NICU	+
Abdeyazdan ^c	2014	Iran	50	m+f	No	Face-to-face education about the NICU environment and preterm infant's care.	Stress	PSS-NICU	+
Beheshipour ^c	2014	Iran	100	m+f	Yes	Parents received face-to-face information about the NICU, their preterm infant's condition, resources for spouse support, and problem solving strategies.	Stress	PSS-NICU	+
Hoffenkamp	2015	Netherlands	294	m+f	Yes	VIG provided parents with positive feedback on video recordings with their preterm infants.	Anxiety	STAI	0
Balbino	2016	Brazil	132	m+f	No	The Patient and Family-Centered Care Model promoted the inclusion of the family in the NICU and infants' care.	Stress	PSS-NICU	+
Barlow	2016	UK	31	m+f	Yes	VIG provided parents with positive feedback on video recordings with their infants.	PTSD, Stress, Anxiety	PSI, PC-PTSD, HADS	0
Welch	2016	USA	115	m	Yes	Family Nurture Intervention provided mothers and preterm infants with calming activities.	Anxiety	STAI	+
Goudarzi	2016	Iran	42	m	Yes	Face-to-face education about intestinal disease and care for mothers of infants with colostomies.	Anxiety, Stress	DASS	0
Valizadeh	2016	Iran	99	m	Yes	Mothers of preterm infants oriented to the NICU environment through a film or booklet.	Anxiety	STAI, CAQ	+
Psychotherapy									
Jotzo ^c	2005	Germany	50	m	No	One-off crisis intervention combined with additional professional psychological aid for mothers of preterm infants.	PTSD	IES	+
Bernard ^c	2011	USA	50	m	Yes	Cognitive-behavioral therapy for mothers of preterm infants.	PTSD	DTS, SASQR	0

Table 1 (continued)

First author	Year	Country	Subjects enrolled	Parents ^a Randomized	Intervention	Distress measures	Instruments	Significant difference ^b
Shaw	2013	USA	105	m	Yes	TF-CBT, cognitive processing therapy, and psychoeducation for mothers of preterm infants.	Anxiety, PTSD DTS, BAI	+
Shaw	2014	USA	105	m	Yes	TF-CBT for mothers of preterm infants.	Anxiety, PTSD DTS, BAI	+
Cano Giménez	2015	Spain	134	m+f	No	Five-step individualized intervention program delivered by a psychologist to parents of term infants.	Stress PSS-NICU	+

Interventions—*COPE* Creating Opportunities for Parent Empowerment, *DMT* Decision Making Tool, *FIC* Family Integrated Care, *GFCC* Guided Family-Centered Care, *MTP* Mother Infant transaction program, *NEDP* Neonatal Early Discharge and Family Support Program, *NIDCAP* Newborn Individualized Developmental Care and Assessment Program, *PBIP* Parent Baby Interaction Program, *TF-CBT* Trauma-focused cognitive behavioral therapy, *VIG* Video Interaction Guidance

Instruments—*BAI* Beck Anxiety Inventory, *CAQ* Cattel's Anxiety Questionnaire, *DASS* Depression Anxiety Stress Scale, *DTS* Davidson Trauma Scale, *IES* Impact of Events Scale, *PC-PTSD* Primary Care-Post-traumatic Stress Disorder, *PPQ* Perinatal Posttraumatic Stress Disorder Questionnaire, *PSI* Parenting Stress Index, *PSS-NICU* Parental Stressor Scale: Neonatal Intensive Care Unit, *PSS* Parental Stressor Scale, *SASRQ* Stanford Acute Stress Reaction Questionnaire, *SCL-90-R* Symptom Check List-90-Revised, *SPSQ* Swedish Parenthood Stress Questionnaire, *STAI* State-Trait Anxiety Inventory

^aMothers (m), Fathers (f), Both (m + f)

^bSignificant improvement (+), Significant worsening (−), No significant difference (0)

^cIncluded in meta-analysis of long-term (primary) outcome

^dIncluded in meta-analysis of pre-discharge (secondary) outcome

Study characteristics

The 58 studies we reviewed enrolled 5887 parent subjects (Table 1). The median year of publication for this body of literature was 2013. Twenty studies were conducted in North America, 16 in Europe, nine in Iran, seven in Asia, three in Australia, and three in Brazil.

Studies predominantly enrolled mothers and parents of preterm infants. Thirty-six studies tested interventions exclusively on mothers while three studies enrolled only fathers and 19 studies enrolled both mothers and fathers. Six studies permitted enrollment of full-term infants.

Intervention classification

We classified 46 distinct interventions into four broad categories: (1) changing NICU medical care; (2) complementary/alternative medicine; (3) family-centered instruction; and (4) psychotherapy.

We classified as “Changing NICU medical care” 11 studies that altered parents’ exposure to the organization or delivery of medical treatment performed by nurses or physicians as compared to contemporaneous local standards of care. Interventions in this class primarily targeted other outcomes alongside distress. Interventions that changed infant rooming or visiting conditions aimed to enhance parent–infant bonding. Parent-to-parent support groups provided families with social resources during a uniquely challenging experience [32]. Interventions that integrated parents directly in their infant’s medical care empowered parents to fulfill their parental role [33]. Parent–professional communication interventions aimed to improve comprehension or shared medical decision making [34].

We drew on classifications by the National Center for Complementary and Integrative Health to determine eligibility in the category “Complementary/alternative medicine” [35]. We included 12 studies that introduced mind–body modalities originating outside the allopathic medical tradition. Interventions in this class typically were designed to decrease stress. Mind–body modalities included maternal acupuncture, journal writing, relaxation techniques, music interventions, infant massage, and parent–infant skin-to-skin contact. Consistent with the recent growth of complementary/alternative medicine use among the general population, these publications were the most recent, with a median publication year of 2015 [36].

The most frequently studied class of intervention was formed by multifaceted programs of “Family-centered instruction”. These interventions in 30 studies predominantly focused on the developmental trajectory of premature infants. In their meta-analysis, Benzie et al. developed a classification for the components of this intervention category comprised by (1) parent psychosocial

support; (2) parent education in the form of either information alone, guided infant observation, or active parent involvement with professional feedback; and (3) infant developmental support [21].

Finally, in five “Psychotherapy” studies, licensed mental health professionals administered psychological therapy, frequently an application of cognitive-behavioral therapy explicitly designed to remedy distress symptoms, face-to-face with parents during their child’s NICU hospitalization.

Distress instruments

Stress was the most frequently assessed aspect of distress, measured in 25 reports using the Parental Stressor Scale: NICU and in 10 reports using the Parenting Stress Index. Seventeen studies measured anxiety using the State-Trait Anxiety Inventory. Post-traumatic stress symptoms were assessed using the Perinatal Post-traumatic Stress Disorder Questionnaire in four studies and the Davidson Trauma Scale in three studies. All reported instruments for stress, anxiety, and post-traumatic stress are listed in Table 1.

Randomized studies meta-analysis

When assessed for our primary outcome, the effect size at the latest-reported time point, NICU-based interventions modestly decreased stress- or trauma-related distress in NICU parents at large. The cumulative effect was a one-third standard deviation reduction in distress symptoms across multiple psychometric measures ($N = 22$; SMD: -0.34 , 95% CI $(-0.51, -0.17)$; $p < 0.001$) with a high level of heterogeneity among study effect estimates ($I^2 = 72.7\%$, Cochran’s Q $p < 0.001$) (Fig. 2). The bulk of analyzed randomized studies did not exhibit evidence of reporting bias, with a negative Egger’s test ($p = 0.09$) and study effect sizes fairly symmetrically distributed in a funnel plot (Fig. 3). The three outliers on the funnel plot represent two studies conducted in Iran that we excluded in a post-hoc sensitivity analysis described below.

In subgroup analyses of randomized studies, interventions categorized as “Complementary/alternative medicine” ($N = 4$; SMD: -0.47 [$-0.83, -0.12$]; $p < 0.01$) and “Family-centered instruction” ($N = 13$; SMD: -0.37 [$-0.59, -0.15$]; $p = 0.001$) reduced parental distress symptoms. “Changing NICU medical care” interventions ($N = 4$; SMD: -0.08 [$-0.44, 0.28$]; $p > 0.05$) did not decrease parental distress overall. Only one randomized “Psychotherapy” study was eligible for quantitative synthesis; thus, this category could not be assessed in this analysis.

When assessed for our secondary outcome, randomized studies reporting treatment effects prior to NICU discharge

did not decrease distress symptoms, neither overall ($N = 9$; SMD -0.08 [$-0.24, 0.09$]; $p > 0.05$) nor within any intervention classification subgroup ($p > 0.05$). These studies did not exhibit evidence of reporting bias, with a symmetric funnel plot (not shown) and a negative Egger’s test ($p = 0.7$).

Effects in mothers and fathers

Family-centered instruction interventions decreased distress symptoms in mothers and fathers by similar magnitudes (mothers’ SMD: -0.5 [$-0.85, -0.14$], $p < 0.01$; fathers’ SMD: -0.32 [$-0.64, -0.01$], $p < 0.05$). Among randomized studies, only studies in this class distinctly reported results for fathers. These studies predominantly enrolled parents of preterm infants.

Long-term distress reduction

The furthest time of distress measurement within studies ranged from 1 day to 9 years in the 21 studies that specified timing (median 90 days, interquartile range [10 days, 1 year]). Half of the 16 randomized studies specifying timing measured distress symptoms 6 months or later after intervention. Overall, these interventions decreased long-term parental distress symptoms (SMD: -0.22 [$-0.38, -0.07$]; $p < 0.005$) with a low level of heterogeneity ($I^2 = 18\%$, Cochran’s Q $p = 0.28$).

Post-hoc sensitivity analysis

The two eligible randomized studies conducted in Iran produced considerably larger effect sizes favoring intervention than studies conducted elsewhere. A post-hoc sensitivity analysis excluding these studies yielded results consistent with our initial findings. The remaining interventions reduced parental distress ($N = 20$; SMD -0.19 [$-0.29, -0.09$], $p < 0.001$), and, among them, complementary/alternative medicine and family-centered instruction interventions decreased distress ($p < 0.01$).

Non-randomized studies meta-analysis

Assessed for our primary outcome, the effect size at the latest-reported time point, ten nonrandomized studies eligible for meta-analysis reduced parental distress overall (SMD: -0.99 , 95% CI $[-1.56, -0.41]$, $p = 0.001$) with a high level of heterogeneity ($I^2 = 91.4\%$, Cochran’s Q $p < 0.001$) (Supplemental Figure A). A symmetric funnel plot of nonrandomized studies (Supplemental Figure B) as well as a negative Egger’s test ($p = 0.98$) suggest the absence of evident reporting bias. “Complementary/alternative medicine” and “Family-centered instruction” interventions in

Fig. 2 Forest plot of randomized studies. SMD standardized mean difference

nonrandomized studies decreased distress symptoms ($p < 0.05$).

Discussion

We believe this is the first comprehensive synthesis of the diverse body of literature on NICU-based interventions for parental distress. To produce a synthesis applicable to

NICU parents at large, we analyzed controlled studies of the effect of NICU interventions on stress- or trauma-related distress, regardless of treatment modality, parent sex, or newborn gestational age. We classified a diverse array of treatments into broad categories, and we quantified their effectiveness, altogether and within classes.

In light of recommendations to provide psychosocial support to all NICU parents, this review serves clinicians and health systems by highlighting priorities for

Fig. 3 Funnel plot of randomized studies. Three outlier effect sizes represent two studies by Behestipour et al. and Mianaei et al. that were excluded in post-hoc sensitivity analysis

implementation. By identifying gaps in the literature, this review serves investigators by identifying opportunities for the further study of available modalities as well as the development of novel treatments.

Overall, NICU interventions produce modest reductions in parental distress symptoms in the long term, though not necessarily when measured prior to hospital discharge. This holds true comparably for mothers and fathers, and the benefits persist in studies measuring distress after 6 months. With these findings, this review encourages NICU parents to expect psychosocial support regardless of their sex or their child's gestational age.

Family-centered instruction interventions, which are multifaceted programs that provide in-hospital parent education, reduce parental distress symptoms and represent the clearest implementation opportunity for health systems not already providing such a program. However, prior reviewers have commented on the challenges of operationalizing this class of intervention owing to the heterogeneity of treatment components, clinical sites, and families [21, 37]. In addition, these programs are designed chiefly to address the developmental needs of preterm infants. Therefore, this category also presents an opportunity for investigators to develop family-centered instruction programs with the flexibility to support parents with infants at any gestational age.

Complementary/alternative medicine approaches represent a promising area for further research because, based on our small and heterogeneous sample, they decrease parental distress. This class of intervention is often relatively inexpensive to implement and enjoys growing acceptance among the public. Four randomized complementary/alternative medicine studies eligible for meta-analysis tested a diverse set of mind-body modalities including acupuncture, journaling, relaxation, and kangaroo care, a form of skin-to-skin parent–infant contact commonly used in the care of

preterm infants [38]. Mind-body modalities might move from the margins of neonatology into the mainstream, for instance, through large-scale, randomized controlled trials of practices such as journaling or meditation.

Interventions that changed NICU medical care had an overall null effect on parental distress symptoms. This finding suggests that investigators testing changes to medical treatments that impact parents should assess for unintended parental distress, as was evident in a communication intervention reported by Clarke-Pounder et al. [39]. Furthermore, although adult intensive care studies have demonstrated reductions in family distress symptoms following intensive communication interventions, in this study, the few neonatal studies testing communication interventions did not mirror those results [34]. The risk of mortality is considerably greater in adult intensive care than in NICUs, and we can speculate that subsets of NICU parents, such as parents of newborns facing a high risk of death, may experience greater distress reductions than NICU parents at large. This review identifies an opportunity for large-scale studies to test the effect of intensive communication interventions on NICU parental distress.

We were unable to quantitatively synthesize psychotherapy studies in this meta-analysis. We note that four of the five psychotherapy studies we reviewed reported parental distress reductions. Among them, the series of randomized studies by Shaw et al. demonstrated significant reductions in parental distress after trauma-focused CBT; however, they reported results as adjusted estimates, excluding them from our meta-analysis [40, 41]. Future studies could apply meta-regression techniques to appropriately synthesize adjusted results in this body of literature. Current recommendations endorse professional psychotherapy for NICU parents experiencing significant stress- or trauma-related distress during their child's hospitalization [42].

Limitations

This body of literature contains gaps and imbalances with respect to geography, parent sex, infant gestational age, and distress time course, that impose limitations on the generalizability of our findings.

Most studies eligible for systematic review were conducted in North America or Europe, limiting the global generalizability of these findings. We speculate that social resources and norms that vary across regional and cultural contexts will influence treatment effectiveness, a potential explanation for the considerably larger effect sizes found in studies conducted in Iran. Investigators have the opportunity to translate these findings to diverse settings globally.

Fewer than half of reviewed studies enrolled fathers, and many that did failed to report outcomes for fathers

distinctly. Fathers have an important role to play in the social-emotional development of high-risk infants and in the well-being of their family. Therefore, the omission of fathers from this body of literature has consequences not only for fathers but for their partners and their children, as well [43]. In light of our finding that fathers respond to interventions as well as mothers do, investigators must develop and test interventions designed to address the psychosocial needs of both mothers and fathers.

Only one in ten eligible studies enrolled parents of full-term infants, thereby omitting a class of parents no less susceptible to stress- and trauma-related distress [3]. While preterm infants are typically hospitalized because of problems related to their developmental immaturity, term infants in an NICU can have medical problems ranging from transient to grave. NICU patients of all gestations can face a wide range of risk for death or disability. Investigators must design interventions that treat NICU parents at large, regardless of their newborn's gestational age.

Several reviewed studies failed to specify the timing of distress observation. Investigators can demonstrate the impact of interventions over variable patterns of distress symptoms by reporting outcomes at multiple discrete timepoints both during the hospitalization and long after discharge.

Finally, our classifying an eclectic array of interventions into broad categories brought disparate treatments together, losing the specificity of interventions as they were implemented in individual studies. Aggregating diverse interventions across varied patient populations, measured by disparate instruments, allowed us to estimate an overall treatment effect for parental distress. Although our effect estimate reflects this body of literature, the heterogeneity of the underlying treatments limits the prediction of an effect size for a given intervention in the future.

Conclusions

In this systematic review and meta-analysis, we found a modest, long-term improvement in parental stress- and trauma-related distress resulting from NICU-based interventions. Based on their effectiveness at reducing distress, we identified opportunities for implementing family-centered instruction programs, and for developing complementary/alternative medicine interventions, each ideally designed to serve NICU parents at large.

By identifying omissions in this body of literature, we highlighted several opportunities for future research. Investigators have the opportunity to develop and test interventions in many regions of the world currently lacking research on NICU parental distress. Future studies ideally will assess the effectiveness of treatments across a lengthy postnatal span. Finally, we found that this field of research

has predominantly limited its scope to the mothers of preterm infants, highlighting an imperative to develop and test psychosocial interventions flexible enough to serve NICU parents at large, including fathers and the parents of critically ill full-term infants.

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Author contributions AS conceptualized, designed, and supervised the study, led the data collection and qualitative synthesis, carried out the quantitative synthesis and final analyses, drafted and revised the final manuscript, and approved the final manuscript as submitted. SF collected data, carried out initial analyses, revised the final manuscript, and approved the final manuscript as submitted. SSN collected data, carried out initial analyses, revised the final manuscript, and approved the final manuscript as submitted. EL collected data, carried out initial analyses, revised the final manuscript, and approved the final manuscript as submitted. DMT conceptualized the study, oversaw the quantitative analysis, revised the final manuscript, and approved the final manuscript as submitted. LZ conceptualized the study, oversaw the qualitative analysis, revised the final manuscript, and approved the final manuscript as submitted.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

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